PCN7

ASSESSING INTERFERON-ALPHA MONOTHERAPY IN PATIENTS WITH ADVANCE OR METASTATIC RENAL CELL CARCINOMA

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OBJECTIVES: The objective was to evaluate the clinical efficacy and safety of interferon-α 2a (IFN) in the treatment of advanced/metastatic renal cell carcinoma in treatment-naïve patients. **METHODS:** Studies were retrieved from Embase, Pubmed, Cochrane, and DARE databases using relevant search strategies. Randomized controlled trials, which compared IFN with other pharmacological interventions/best supportive care (BSC), were included according to prespecified inclusion/exclusion criteria. The outcomes of interest were overall survival (OS), progression free survival (PFS), response rate (RR), and adverse events (AEs). Two reviewers independently extracted data from the included studies. Data were analyzed using RevMan (5). **RESULTS:** Of the 736 studies identified, seven studies met the inclusion criteria. In total, 1147 patients were randomized to IFN, and 1150 were randomized to comparator interventions. Two studies reported comparison with interleukin-2 (IL-2), two with BSC and one each with sorafenib, sunitinib, and temsirolimus. Median OS ranged from 9 to 21.8 months with IFN. Progression-free survival ranged from 1.9 to 5.6 months and overall RR ranged from 4.83% to 12.27% with IFN. Sunitinib had significantly better overall RR ($P < 0.001$), PFS ($P < 0.001$), and OS ($P < 0.01$) compared to IFN. Sorafenib and temsirolimus had better overall RR than IFN ($P < 0.01$). Results of meta- analysis demonstrate that IFN has better overall RR than BSC (OR: 2.51 [95% CI: 0.87, 7.27], $P = 0.089$) and similar RR as IL-2 (OR: 1.09 [95% CI: 0.48, 2.45], $P = 0.836$). The AE profile (gastrointestinal, vascular, infectious, and blood disorders) was similar with IFN and comparators. **CONCLUSIONS:** Survival benefit with IFN-α was lower than the newer therapeutic agents. Anti-angiogenic agents targeting through multiple receptor kinases, such as sunitinib and sorafenib have significantly improved response rates and survival. These agents would be preferred for treatment naïve patients with advanced/metastatic renal cancer.

PCN8

CLINICAL AND ECONOMIC BURDEN OF TOXICITIES ASSOCIATED WITH MONOCLONAL ANTIBODIES FOR METASTATIC COLORECTAL CANCER (MCRC)

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OBJECTIVES: As overall survival improves with newer therapies for mCRC, treatment-limiting toxicities and related costs will be important when evaluating treatment decisions. Little is known about toxicity-related cost of currently available monoclonal antibody treatments. This study was designed to identify cetuximab-, bevacizumab-, and panitumumab-related toxicities and estimate direct costs of treating these toxicities. **METHODS:** A comprehensive literature search was performed to identify English language phase II/III studies of monoclonal antibodies for mCRC. The search utilized PubMed, conference abstracts, treatment guidelines, and product labels. Commonly reported grade 3 and 4 toxicities were identified, and outpatient and inpatient costs were estimated for all toxicities. Outpatient costs were estimated by applying 2010 Medicare reimbursement rates to resource use assumptions (assessed based on in-depth clinical interviews). Inpatient costs were estimated using ICD-9 codes and 2007 Medicare payments from the HCUP database; then were converted to 2010 values using the Consumer Price Index for medical care services. **RESULTS:** Clinically significant toxicities associated with bevacizumab include hypertension, arterial thrombosis, hemorrhage, gastrointestinal (GI) perforation, fistula, and wound healing complication; while treatment-related toxicities associated with cetuximab and panitumumab include skin rash, hypomagnesemia, and infusion reactions, although the incidence of these toxicities differ between the two drugs. Cost of toxicities treated in outpatient setting ranged from $185 (hypertension and skin rash) to $585 (wound-healing complications). Inpatient cost per event for GI perforation is the highest at $32,443, followed by fistula $29,062, arterial thrombosis $20,346, wound healing complication $13,240, hemorrhage $12,956, infusion reaction $10,326, and hypertension $8453, while inpatient cost per event for skin rash and hypomagnesemia is among the lowest at $4424 and $6174, respectively. **CONCLUSIONS:** Monoclonal antibodies have different toxicity profiles and the costs associated with managing these toxicities vary greatly.

PCN9

OBSERVATIONAL STUDY OF PATIENTS WITH NON SMALL CELL LUNG CANCER (NSCLC) TREATED BY ERLOTINIB: CLINICAL PRACTICES AND MAIN OUTCOMES IN FRANCE

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OBJECTIVES: Few data are available about the use of erlotinib in real-life in France for patients with non small cell lung cancer (NSCLC) in a selected population. **METHODS:** An epidemiological multicenter observational study was built in 35 french centers. The study was retrospective (2006 to 2008) and a cohort was created with a follow-up period of 1 year. The main objective was to describe practices, use of erlotinib, response, and adverse events. **RESULTS:** A total of 533 patients (333 males, 200 females) have been included. The histological types were as follows: 330 (62.5%) adenocarcinoma, 107 (20.2%) squamous cell carcinoma, 60 (11.3%) large cell carcinoma, 36 (3.8%) undifferentiated carcinoma. In terms of practice, 502 patients had a first line chemotherapy (81% a doublet, 11% three drugs, 8.2% one drug). Among them, 61.2% received a second line of treatment (83.4% one drug, 15.7% two drugs and 0.9% three drugs), 17.6% received a third line (91% one drug). Erlotinib was prescribed a first line treatment (n = 30; 5.6%), second line treatment (n = 190; 35.6%), third line (255; 47.8%), fourth line, and more (n = 50; 9.3%) and as a maintenance therapy (n = 9; 1.7%); the stage at treatment initiation were stage I–II (1.2%), IIIA (3.8%), IIIB (5.3%), and IV (89.7%). For the first line, the median duration of erlotinib treatment was 123 days (d) in second line 98 d, in third line 77 d, in maintenance 127 d. Global response rate was 20% with a maximum of 32% in first line and 33% in maintenance. Grade III adverse events occurred in 11.5% of patients and grade IV in 3.4%. **CONCLUSIONS:** Erlotinib was widely used in France in 2[d] and 3[d] line treatment with a good response rate and tolerance. Adenocarcinoma is the main indication.

PCN10

EXPLORATIVE ANALYSIS ABOUT THE POTENTIAL OF A LARGE GPS LONGITUDINAL DATABASE ON SEARCHING CAUSAL ASSOCIATIONS AMONG PATHOLOGIES

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OBJECTIVES: The main objective of this study was to analyze different approaches and methods to explore potential causal associations among prevalent pathologies. We have focused on diabetes mellitus (DM) and its well-known association with incident neoplasia. **METHODS:** For this retrospective cohort study, data were obtained from CSD LPD, a General Practitioner's longitudinal database. We have evaluated the risk of neoplasia incidence among people with diabetes mellitus compared with those without this pathology, in patients who had no reported history of benign or malign neoplasia at the start of the follow-up on January 2006. For the DM group, patients with at least one diagnosis of DM from January 2005 to December 2005 have been selected, while for the DM-free group, patients without a diagnosis of DM and a date of registration in the GPs office before January 2006 have been selected. Both groups have been followed up for 48 months. **RESULTS:** During the selection period, 45.121 (3.4%) patients with a diagnosis of DM (females: 22.330, males: 22.791) and 1.290.597 (96, 6%) patients without a diagnosis of DM (females: 690.462, males: 600.135) have been selected. During the follow-up 6.648 and 80.880 incident cases of neoplasms have been documented from the DM and DM free groups respectively. The mean follow-up duration was 43 and 45 months for the DM and the DM-free groups respectively. **CONCLUSIONS:** The selected cohort has shown to match quite well with general population in terms of gender and age. The estimated prevalence of diabetes also matches with the one of the general population. Statistical analysis has shown an adjusted (for age and sex) hazard ratio of 1,88 (95% CI 1,83–1,93) suggesting an association between DM and incident neoplasms, evidencing that GPs longitudinal databases could be a valid instrument for evaluating causal association among prevalent pathologies.

PCN11

GEFITINIB COMPARED WITH DOUBLET CHEMOTHERAPY FOR FIRST-LINE TREATMENT OF NON-SMALL-CELL LUNG CANCER (NSCLC): A SYSTEMATIC REVIEW AND ADJUSTED INDIRECT COMPARISON

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OBJECTIVES: Objective response rate (ORR) is an early indicator of successful treatment in patients with NSCLC. This research compared gefitinib with platinum-based doublet chemotherapies for first-line treatment of advanced NSCLC in patients harboring activating epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutations (M+). **METHODS:** Systematic searching of CENTRAL, EMBASE, and MEDLINE for randomized controlled trials (RCTs) comparing ≥2 doublet chemotherapies (carboplatin or cisplatin in combination with either docetaxel, gemcitabine, paclitaxel, pemetrexed, or vinorelbine) for the first-line treatment of advanced NSCLC was completed in May 2009. a meta-analysis was performed on ORR using data from published RCTs of gefitinib versus paclitaxel/carboplatin in EGFR-TK M+ patients. a mixed treatment comparison (MTC) was carried out with doublet chemotherapies in unselected advanced NSCLC patients using paclitaxel/carboplatin as a baseline. Treatment effect was calculated as an odds ratio (OR) with 95% credible interval (95% CrI). a sensitivity analysis was conducted on the inclusion of the gefitinib trials within the MTC. For this analysis, it was assumed that the efficacy of doublet chemotherapy is consistently affected by EGFR-TK mutation status. **RESULTS:** Three RCTs were identified for gefitinib, of which two were comparisons with paclitaxel/carboplatin. Meta-analysis of these two trials gave an estimated ORR favoring gefitinib: OR 4.04, 95% confidence interval: 2.73–5.98. Twenty-nine trials were appropriate for inclusion in the MTC, of which 25 reported ORR. The MTC found no significant difference in ORR among other doublet chemotherapies versus paclitaxel/carboplatin, with the exception of pemetrexed/cisplatin, in patients with predominantly non-squamous tumor cell histology, which was associated with a significantly higher ORR (OR 1.64, 95% CrI: 1.15–2.27). In the sensitivity analysis, ORR was significantly higher with

gefitinib versus all doublet chemotherapies (gefitinib vs. pemetrexed/cisplatin OR 3.05, 95% CrI: 1.58–5.51). **CONCLUSIONS:** This adjusted indirect comparison suggests that gefitinib may have important ORR advantages over other first-line treatments in EGFR-TK M+ patients.

PCN12

EFFICACY OF SECOND LINE TREATMENTS IN PATIENTS WITH METASTATIC HORMONE REFRACTORY PROSTATE CANCER (MHRPC) IS NOT DEMONSTRATED BY PUBLISHED EVIDENCE FROM NON-RANDOMIZED TRIALS

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OBJECTIVES: Standard first-line treatment for patients with mHRPC is Docetaxel(D)-based chemotherapy. Published results from randomized clinical trials of second-line treatments after D failed to provide definitive conclusions about clinical efficacy largely due to paucity of data. This study sought to identify nonrandomized trials of second-line chemotherapy in mHRPC patients pretreated with D and present related survival and clinical benefits. **METHODS:** Pubmed and Embase were used to perform a systematic literature review (SLR) (2000–2010). Both comparative and noncomparative nonrandomized evidence were extracted from prospective and retrospective studies. Targeted population was patients with mHRPC failing previous D-based regimens. End points included overall-survival (OS), progression-free-survival (PFS), and PSA-response rate. **RESULTS:** Among the 825 records screened, 30 studies met the inclusion criteria, two of which were comparative. Of these, 10 addressed rechallenge with D and seven addressed mitoxantrone (MTX); the remaining 18 studies considered various other regimens. Treatment was with either single-agent or combination regimens. Ninety-three percent of studies included <50 patients. PFS and PSA response definitions varied between trials. For studies evaluating rechallenge with D, the median OS and PFS varied from 41 to 76 weeks and from 15 to 39 weeks respectively. For MTX, the median OS and PFS varied from 39 to 48 weeks and 13 to 16 weeks, respectively. For other chemotherapy regimens, the median OS and PFS varied from 51 to 104 weeks and 9 to 17 weeks, respectively. PSA response rates varied from 24% to 70% to D rechallenge, from 4% to 33% to MTX-based regimens and from 0% to 60% to other regimens. **CONCLUSIONS:** The SLR showed a lack of available non-randomized evidence, and among the selected studies, evidence was not strong enough due to small sample sizes, noncomparative nature and variable PFS and PSA response definitions. This literature review demonstrates that it is difficult to infer the clinical efficacy of mHRPC 2nd line chemotherapy.

PCN13

EFFECT OF ZOLEDRONIC ACID AND PAMIDRONATE ON SKELETAL-RELATED EVENTS AND MORTALITY IN WOMEN WITH BONE METASTASES FROM BREAST CANCER IN A MANAGED CARE PLAN: A RETROSPECTIVE DATABASE ANALYSIS

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OBJECTIVES: Patients with breast cancer (BC) and bone metastases are at risk for skeletal-related events (SREs) that are associated with significant morbidity, mortality, and reduced quality of life. The intravenous bisphosphonates (IVBPs) zoledronic acid (ZOL) and pamidronate (PAM) are approved for treating patients with bone metastases from BC. We compared incidence of SREs and mortality in women with BC who received ZOL or PAM, and assessed the long-term benefit of ZOL in a real-world setting. **METHODS:** A claims-based analysis of commercial and Medicare Advantage data from >45 US managed care plans was used to evaluate SRE rates and mortality in patients treated with ZOL or PAM. Inclusion criteria were age >18 years, BC with bone metastasis diagnosis between 01/01/01 and 12/31/06, continuous enrollment in the health plan, no evidence of bone metastasis or IVBP for 6 months before an index date of first receipt of ZOL or PAM. Patients were followed until disenrollment (including mortality) or study completion (12/31/07). Persistency was defined as the absence of a >45-day gap between treatments. SREs were defined as evidence of pathologic fracture, spinal cord compression, and radiotherapy or surgery to bone. **RESULTS:** Among 8757 patients (mean age, 58.1 ± 12.4 years) approximately 30% received ZOL, 15% received PAM, and 55% received no IVBP. Longer persistency with ZOL was associated with lower risk of fracture and of all SREs versus shorter persistency (trend test, $P = 0.0026$ and $P = 0.0216$, respectively). ZOL-treated patients had a moderately lower SRE incidence (36.2 vs. 40.0 per 100 person-years; $P = 0.0707$) and significantly fewer deaths (6.2 vs. 8.9 per 100 person-years; $P = 0.0130$) versus PAM-treated patients. **CONCLUSIONS:** In a real-world assessment of women with bone metastases from BC, ZOL reduced SRE incidence and significantly improved survival versus PAM. Longer ZOL persistency was associated with lower SRE risk, reinforcing the importance of regular monthly ZOL dosing.

PCN14

CLINICAL CONSEQUENCES OF PRIMARY PROPHYLAXIS WITH PEGFILGRASTIM VERSUS FILGRASTIM FOR THE PREVENTION OF FEBRILE NEUTROPENIA IN NON-HODGKIN LYMPHOMA AND STAGE II BREAST CANCER PATIENTS IN GERMANY

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OBJECTIVES: To assess the clinical consequences of primary prophylaxis (PP) with pegfilgrastim versus 6- or 11-day filgrastim (F6, F11) in the prevention of febrile neutropenia (FN) in non-Hodgkin lymphoma (NHL) patients receiving CHOP-14 chemotherapy and in breast cancer (BC) patients receiving TAC chemotherapy in Germany. **METHODS:** A lifetime Markov model was developed, consisting of two phases: 1) on-chemotherapy phase (OCP), where model cycle length equals chemotherapy cycle length (CHOP-14:14 days, TAC: 21 days), and 2) post-chemotherapy phase (PCP) with annual model cycles. PP is defined as prophylaxis initiated with the first chemotherapy cycle. Cycle 1 FN risk with no prophylaxis (NP) was estimated to be 21% for NHL CHOP-14 and 14% for BC TAC. All cycle relative risk of FN using PP with pegfilgrastim versus no PP, F6, and F11 was 0.25, 0.87, and 0.61. FN case fatality was estimated (NHL: 8.9%; BC: 3.6%). In PCP, all-cause mortality was estimated from German life-tables; NHL and BC mortality from US data; patients experiencing FN were assumed to have higher mortality due to reduced chemotherapy dose intensity. All inputs were estimated from clinical trials and published literature. The model estimates life-years, number of FNs, and number needed to treat (NNT) to prevent an FN. **RESULTS:** NNT to prevent an FN were 1.3, 6.2, 2.2 in NHL; 2.3, 11.1, 4.0 in BC for Pegfilgrastim, F6, and F11 compare to NP. Overall, FN episodes per patient were 0.15, 0.76, and 0.47 in NHL; 0.09, 0.43, and 0.27 in BC. Per-patient life-months gained using PP with Pegfilgrastim were 3.4 and 1.8 versus F6 and F11, respectively in NHL, and 2.2 and 1.2 in BC. **CONCLUSIONS:** Primary prophylaxis with pegfilgrastim results in a lower NNT, fewer FN events, and more life-years than with 6-day filgrastim or 11-day filgrastim in both NHL and BC.

PCN15

SYSTEMATIC REVIEW OF LAPATINIB PLUS LETROZOLE WITH OTHER FIRST LINE TREATMENTS FOR HORMONE POSITIVE (HR+) HER2+ ADVANCED OR METASTATIC BREAST CANCER (MBC)

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OBJECTIVES: To undertake a systematic review of lapatinib plus letrozole (LAP + LET) with other first-line treatments for HR+ HER2+ advanced or MBC in postmenopausal women who have not received prior therapy for advanced or metastatic disease. **METHODS:** Seven databases were searched through January 2009 for randomized controlled trials. Relevant interventions were lapatinib (alone/in combination), aromatase inhibitors (letrozole (LET), anastrozole (ANA), exemestane (EXE)), tamoxifen (TAM), and trastuzumab (TRAS) (alone/in combination). Outcomes included overall survival (OS), progression-free survival (PFS), time to progression (TTP), and objective response rate (ORR). From the available evidence, it was possible to directly compare LAP + LET with LET. Using a network meta-analysis, LAP + LET could be indirectly compared with the four other interventions. **RESULTS:** Eighteen studies (62 papers) met the inclusion criteria. LAP + LET was significantly superior to LET based on a direct head-to-head study in terms of PFS/TTP and ORR. In the indirect comparison with LAP + LET, TAM (hazard ratio [HR] = 0.45 [95% CI: 0.32, 0.65]), EXE (HR = 0.52 [0.34, 0.79]), and ANA (HR = 0.53 [0.36, 0.80]) scored significantly worse in terms of PFS/TTP and ORR (TAM: odds ratio [OR] = 0.25 [0.12, 0.53], ANA: OR = 0.27 [0.12, 0.58], EXE: OR = 0.47 [0.20, 1.09]). LAP + LET also seemed better, although not significantly, in terms of OS versus TAM: HR = 0.74 (0.49, 1.12), EXE: HR = 0.65 (0.39, 1.11), and ANA: HR = 0.71 (0.45, 1.14). LAP + LET when indirectly compared with TRAS + ANA, seemed to be better in terms of OS (HR = 0.85 [0.47, 1.54]), PFS/TTP (HR = 0.89 [0.54, 1.47]) and ORR (OR = 0.92 [0.24, 3.48]), although, none of these results were significant. **CONCLUSIONS:** Using indirect methods, LAP + LET appeared to be the best treatment in this HR+ HER2+ patient population. However, the results are based on a network analysis for which the basic assumptions of homogeneity, similarity, and consistency were not fulfilled. Therefore, despite the fact that these are the best available data, the results need to be interpreted with caution.

PCN16

MIXED TREATMENT COMPARISON OF BEVACIZUMAB-BASED THERAPIES RELATIVE TO DOUBLET-CHEMOTHERAPY COMBINATIONS TO ESTIMATE THE RELATIVE EFFICACY IN PROGRESSION-FREE SURVIVAL FOR TREATMENT OF FIRST-LINE ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC)

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OBJECTIVES: To compare the efficacy in progression-free survival (PFS) of bevacizumab plus cisplatin and gemcitabine (BCG) and bevacizumab plus carboplatin and paclitaxel (BCP), relative to doublet-chemotherapy combinations for the treatment of